

## LYME DISEASE

### ✓ DISEASE AND EPIDEMIOLOGY

#### Clinical Description:

Symptoms can be vague and diagnosis can be difficult. Clinical manifestations occur in three stages:

##### **Early localized:**

About 60-80% will have a skin lesion that begins as a red macule or papule at the site of the tick bite and expands slowly in a circular manner, often with a central clearing. This skin lesion is referred to as a “bulls-eye” rash or erythema migrans (EM). EM may be single or multiple. For purposes of surveillance, a single primary lesion must reach 5 cm or 2 inches in diameter to be considered EM. The center of the rash may be vesicular or necrotic. The early localized stage usually occurs within 3-32 days following the tick bite (average 7 days).



Other clinical manifestations include malaise, fatigue, fever, headache, stiff neck, myalgia (muscle aches), arthralgia (joint pain), and/or lymphadenopathy (swollen lymph nodes). The initial disease may last for weeks in untreated patients; symptoms may be intermittent and variable. In some patients, this initial presentation will be inapparent.

##### **Early disseminated:**

If untreated, approximately 5% of patients may develop chronic disease weeks to months after the initial symptoms. Early disseminated disease can occur several weeks after the primary tick bite and presents as multiple erythema migrans, usually smaller than the primary lesion. Other symptoms may include arthralgia, meningitis, neurologic abnormalities such as facial or Bell's Palsy and carditis (see Case Definition).

##### **Late disease:**

Arthritis is the typical manifestation of late disease. Since only 60-80% of cases have a visible acute (or early localized) presentation, late disease may be the first indicator of Lyme disease. Patients with untreated infection may begin to have intermittent bouts of arthritis, with severe joint pain and swelling, particularly in the large joints and knees. Other arthritic presentations are not indicative of Lyme disease.

#### **Causative Agent:**

Lyme Disease is a zoonotic disease caused by the tick-borne spirochete, *Borrelia burgdorferi*.

#### **Differential Diagnosis:**

The differential diagnosis for acute Lyme disease includes dermatologic conditions such as insect bites. For chronic (late disease) Lyme disease, the differential includes MS, ALS, arthritis, CFS, ADHD, fibromyalgia, and other difficult-to-diagnose multi-system syndromes.

## **Laboratory identification:**

Laboratory testing is poorly standardized and test results should be interpreted with caution. Testing is generally performed through a two-step process, similar to HIV/AIDS. Initially, serological tests, such as an enzyme immunoassay (EIA) or an indirect immunofluorescence assay (IRA), are used to screen patients. Samples that are reactive or equivocal on the screening tests are then tested with a Western Blot. The usefulness of PCR in routine management of Lyme disease cases has yet to be verified.

### **Appropriate testing algorithm:**

Initially, a total immunoglobulin serology test should be performed. If reactive, the following tests should be performed to confirm the diagnosis:

- a. If the symptom onset is <30 days, perform BOTH an IgM Western Blot and IgG Western Blot.
- b. If the symptom onset is >30 days, perform an IgG Western Blot, or test paired acute- and convalescent-phase serum samples.

### **Understanding the tests:**

- Samples may fail to react when the disease is in its early stages, yielding a false negative result.
- Samples may fail to react when a patient is treated early in the disease, also yielding a false negative result.
- The antibodies (IFA or EIA/ELISA) can cross react in patients with antibodies to other spirochetal infections, such as Rocky Mountain spotted fever, syphilis, relapsing fever, leptospirosis, certain viral infections, such as HIV, varicella, Epstein-Barr or certain autoimmune diseases, such as infectious mononucleosis, lupus, or rheumatoid arthritis, yielding a false positive result.
- Generally, the test sensitivity increases as the disease progresses, but some patients fail to seroconvert even during the chronic phase of the illness.
- IgM Western Blots should not be used to support a diagnosis for Lyme disease when disease manifestations have existed for longer than one month.

### **Sensitivity of the tests:**

- During the first four weeks of infection, serodiagnostic tests are insensitive and are not generally recommended.
- An IgM EIA or ELISA that uses a recombinant antigen is more sensitive than those using whole cell ELISA.
- An IgG Western Blot that uses VIsE or C6 recombinant antigens increases the sensitivity of the test.
- Culture is difficult and not recommended.

**Treatment:**

	<b>Adults*</b>	<b>Children</b>
<b>EM and early localized disease</b>	Doxycycline** 14-21 day course of oral agents	Under 8 years of age: Amoxicillin** 14-21 day course of oral agents
<b>Early disseminated and late disease</b>	28 day course of oral agents	21-28 day course of oral agents depending on symptoms
<b>Neurological symptoms and Carditis</b>	IV Ceftriaxone IV Penicillin 14-28 day course of treatment	IV Ceftriaxone IV Penicillin 14-28 day course of treatment

\*Tetracyclines are contraindicated in pregnant women.

\*\*Cefuroxime axetil or erythromycin can be used in those allergic to penicillin or tetracycline.

For specific dosages, refer to the 2006 Guidelines for treatment developed by the Infectious Diseases Society of America.

**Case fatality:**

If untreated, Lyme disease can cause chronic illness, but is rarely fatal.

**Reservoir:**

Lyme disease is tick-borne disease. Vectors include the black-legged tick, *Ixodes scapularis* (formerly *I.dammini*) in the eastern and midwestern United States and the black-legged tick, *I. pacificus*, in the western United States and is present in Utah. White-tailed deer are an important maintenance host. Dogs, cattle, and horses are all susceptible to this disease.

**Transmission:**

Tick-borne. The length of time of tick attachment for transfer of the spirochete is unknown, but in most cases, the tick must be attached for 24-48 hours or more before the Lyme disease bacterium can be transmitted. Maternal transmission of this disease is possible, but has not been well-documented.

**Susceptibility:**

All people are susceptible. Reinfection can occur in people who were treated with antibiotics early in the disease cycle.

**Incubation period:**

The incubation period from tick bite to EM ranges from 3-32 days with an average of 7-14 days.

### **Period of communicability:**

There is no evidence of person-to-person transmission. There are rare cases of congenital transmission, but without adverse outcomes.

### **Epidemiology:**

Lyme disease occurs primarily in three geographic regions of the United States. Largest numbers of cases occur along the Atlantic coast, north central United States (Wisconsin and Minnesota), and the Pacific coast (Oregon and California). It has been reported from 47 states. Few cases of Lyme disease are described as being possibly linked to Utah. Lyme disease is the most common vector-borne disease in North America. While Utah has tick reservoirs capable of supporting Lyme disease, cases acquired in Utah are rare.

## **PUBLIC HEALTH CONTROL MEASURES**

### **Public health responsibility:**

- Determine the probable source (location) of the infection.
- Determine if and where transmission is occurring in Utah.
- Remember that due to the small size of this tick, many patients will not recall a tick bite during the investigation.
- Classify cases according to Centers for Disease Control and Prevention (CDC) and Council for State and Territorial Epidemiologists (CSTE) criteria so that accurate records on Lyme disease can be maintained at the national level.
- If Lyme disease transmission is found to occur in Utah, public health will educate the public about the mode of tick transmission and the ways to avoid infection.
- Educate physicians on diagnosis, testing and reporting.

### **Prevention:**

Avoid tick-infested areas when feasible. Wear light-colored clothing with long sleeves and long-legged pants. Tuck pant legs into socks to prevent ticks from crawling up legs. Apply an insect repellent, such as DEET, to your skin and permethrin on clothing.

There is currently no licensed vaccine available against Lyme disease.

### **Chemoprophylaxis:**

Routine use of antimicrobial prophylaxis is not recommended. The risk of Lyme disease following a tick bite in Utah is low.

### **Vaccine:**

There is currently no licensed vaccine available against Lyme disease.

### **Isolation and quarantine requirements:**

**Isolation:** None

**Hospital:** Standard body substance precautions.

**Quarantine:** Patients with active Lyme disease should not donate blood.

## ✓ CASE INVESTIGATION

### Reporting:

Lyme disease is a reportable disease in Utah. Lyme disease is a nationally notifiable disease.

### Case definition:

#### **Lyme Disease (2011):**

##### **Clinical Presentation**

A systemic, tickborne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The best clinical marker for the disease is erythema migrans (EM), the initial skin lesion that occurs in 60-80% of patients.

For purposes of surveillance, EM is defined as a skin lesion that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach greater than or equal to 5 cm or 2 inches in size across its largest diameter. Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. The diagnosis of EM must be made by a physician. Laboratory confirmation is recommended for persons with no known exposure.

For purposes of surveillance, late manifestations include any of the following when an alternate explanation is not found:

- Musculoskeletal system. Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints. Manifestations not considered as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis. Additionally, arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement.
- Nervous system. Any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis. Encephalomyelitis must be confirmed by demonstration of antibody production against *B. burgdorferi* in the Cerebral Spinal Fluid (CSF), evidenced by a higher titer of antibody in CSF than in serum. Headache, fatigue, paresthesia, or mildly stiff neck alone, are not criteria for neurologic involvement.
- Cardiovascular system. Acute onset of high-grade (2<sup>nd</sup> or 3<sup>rd</sup> degree) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis. Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.

## Laboratory Evidence

For the purposes of surveillance, the definition of a qualified laboratory assay is:

- A positive culture for *B. burgdorferi*.
- Two-tier testing interpreted using established criteria [1], where
  - a. Positive IgM is sufficient only when  $\leq 30$  days from symptom onset.
  - b. Positive IgG is sufficient at any point during illness.
- Single-tier IgG immunoblot seropositivity using established criteria [1-4].
- CSF antibody positive for *B. burgdorferi* by Enzyme Immunoassay (EIA) or Immunofluorescence Assay (IFA), when the titer is higher than it was in serum.

A two-step approach for active disease and for previous infection using a sensitive enzyme immunoassay (EIA) or immunofluorescent assay (IFA) followed by a Western immunoblot is the algorithm of choice. All specimens positive or equivocal by a sensitive EIA or IFA should be tested by a standardized Western immunoblot. Specimens negative by a sensitive EIA or IFA need not be tested further. When Western immunoblot is used during the first four weeks of disease onset (early LD), **both** immunoglobulin M (IgM) and immunoglobulin G (IgG) procedures should be performed. **A positive IgM test result alone is not recommended for use in determining active disease in persons with illness greater than one month's duration because the likelihood of a false-positive test result for a current infection is high for these persons.** If a patient with suspected early LD has a negative serology, serologic evidence of infection is best obtained by testing of paired acute- and convalescent-phase serum samples. Serum samples from persons with disseminated or late-stage LD almost always have a strong IgG response to *Borrelia burgdorferi* antigens. [1]

## Exposure

Exposure is defined as having been ( $\leq 30$  days before onset of EM) in wooded, brushy, or grassy areas (e.g., potential tick habitats) in a county in which Lyme disease is endemic. A history of tick bite is not required.

## Disease endemic to county

A county in which Lyme disease is endemic is one in which at least two confirmed cases have been acquired in the county or in which established populations of a known tick vector are infected with *B. burgdorferi*.

## Detailed definitions for case classification

*Confirmed:*

- A case of EM with a known exposure (as defined above), or
- A case of EM with laboratory evidence of infection (as defined above) and without a known exposure or
- A case with at least one late manifestation that has laboratory evidence of infection (as defined above).

*Probable:*

Any other case of physician-diagnosed Lyme disease that has laboratory evidence of infection (as defined above).

*Suspected:*

- A case of EM where there is no known exposure (as defined above) and no laboratory evidence of infection (as defined above) or
- A case with laboratory evidence of infection but no clinical information available (e.g., a laboratory report)

Lyme disease reports will not be considered cases if the medical provider specifically states this is not a case of Lyme disease, or the only symptom listed is “tick bite” or “insect bite.”

**Case Investigation Process:**

- Fill out an investigation form on each case of Lyme disease. Some of the information on this form must be provided by a clinician or other medical personnel. The patient cannot answer the medical questions appropriately.
- IF the clinician indicates that the patient has erythema migrans, contact the patient and collect information on possible locations of infection.

**Outbreaks:**

An outbreak will be defined as two (2) or more cases of locally acquired Lyme disease in a county in a 12-month period.

**Identification of case contacts:**

None

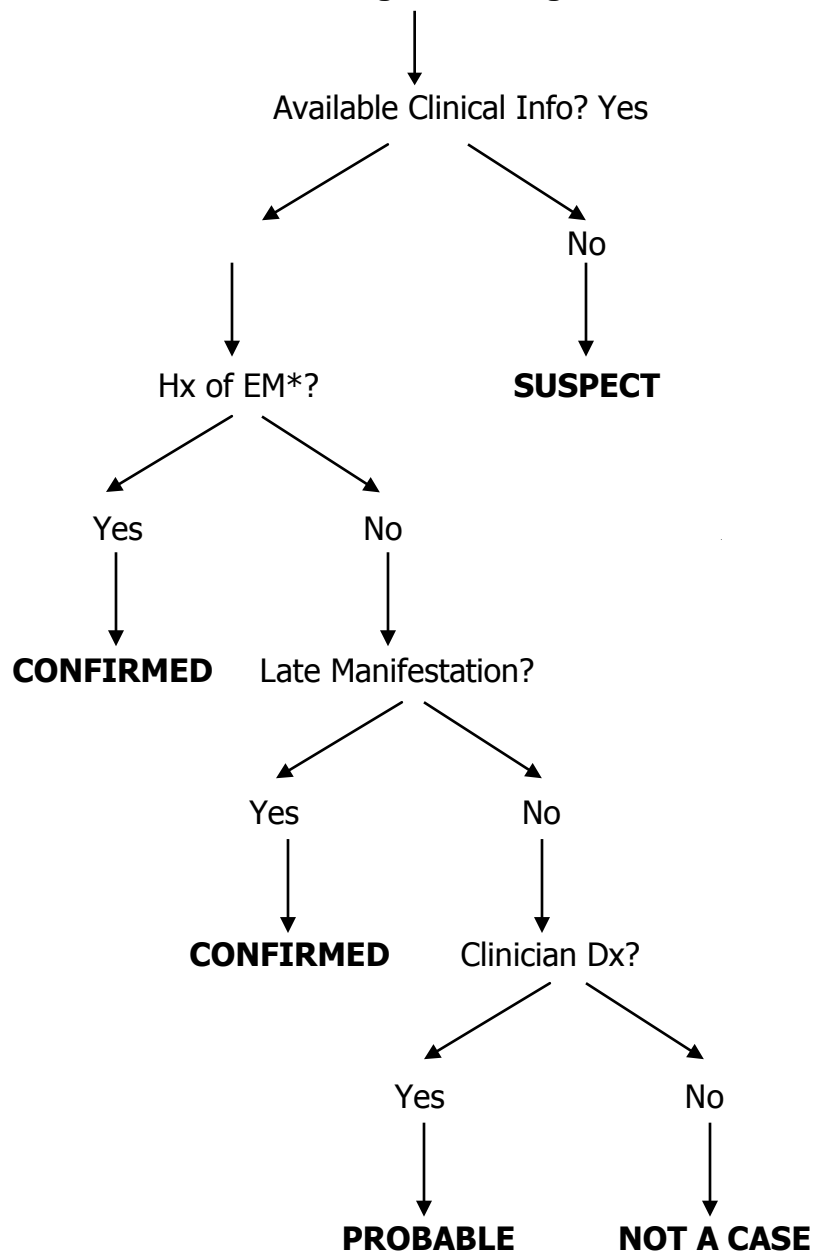
**Case contact management:**

None

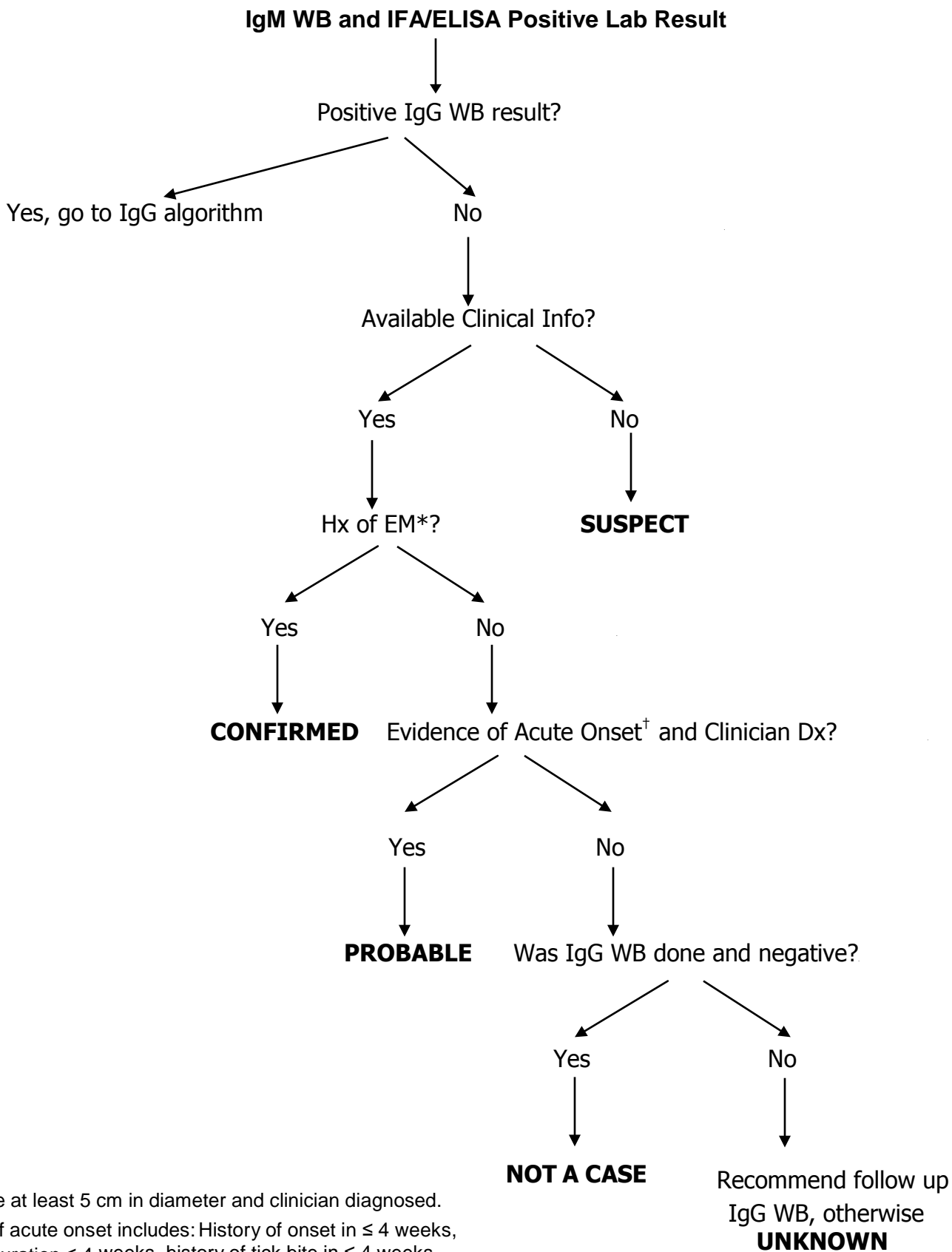
### Interpretation of Lyme Disease Laboratory Test Results for Determination of Case Status, Utah 2010

Reported Lab Result(s)			Action
IFA/ELISA	IgM WB	IgG WB	
+ or equivocal	+, - or missing	+	Follow IgG WB interpretation algorithm
+	+	Missing or -	Follow IgM WB interpretation algorithm
Missing	+, - or missing	+	Follow IgG WB interpretation algorithm
Missing	+	-	If clinical information is available and suggests chronic illness, it is NOT A CASE. If clinical information is consistent with acute illness (or if you are unsure), recommend two-tiered (with IgG and IgM WB) testing. Otherwise UNKNOWN.
Missing	+	Missing	Determine if IFA/ELISA and IgG WB testing were done. If not, recommend two-tiered testing. Otherwise UNKNOWN.
+ or equivocal	Missing	Missing	Determine if WB testing was done. If not, recommend two-tiered (with IgG and IgM WB) testing if patient has compatible illness. Otherwise UNKNOWN.
+ or equivocal	-	-	NOT A CASE unless patient has compatible illness and is early in course of illness (< 4 weeks since onset). If early illness, recommend repeat two-tiered testing or paired serology.
-	-	-	NOT A CASE unless patient has a clinician diagnosis or compatible illness and is within 2-3 weeks of onset/exposure, phycompatible illness. If so, recommend repeat two-tiered testing.

### IgG WB and IFA/ELISA OR Single Tiered IgG WB Positive Lab Results



\*EM must be at least 5 cm in diameter and clinician diagnosed.



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